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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,003	10/26/2000	M. Rigdon Lentz	LEN 101 CIP CON	7721

23579 7590 10/24/2002

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EXAMINER	
BIANCO, PATRICIA	
ART UNIT	PAPER NUMBER
3762	

DATE MAILED: 10/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No. 09/699,003	Applicant(s) LENTZ, M. RIGDON	
	Examiner Patricia M Bianco	Art Unit 3762	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 October 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3 & 4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Non-Final Rejection* .

PBianco 10/17/02

DETAILED ACTION

Drawings

1. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the following must be shown or the feature(s) canceled from the claim(s): absorbent column (claim 16) or column (claims 10 &19); means for administering radiation to the tissue (claim 21); device having filters having pores of different sizes or geometries (claim 15); a capillary membrane filter (claim 13) and a parallel plate filter (claim 14). Also, with respect to the "kit" (claims 22-29), the generally accepted showing of a kit is a packaging enclosing or holding all of the components of the kit (i.e. device and selected agent) should be shown as a figure. No new matter should be entered.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

2. The drawings are objected to because reference number "38" is indicated on figure 1 to be "venous pressure" and in the specification is called "pressure gauge." Consistency should be maintained when discussing and illustrating structural features for clarity. The use of one name should be used in both the figures and specification. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

3. The use of the trademarks has been noted in this application. It should be capitalized wherever it appears **and** be accompanied by the generic terminology. It appears that numerous trademarks have been recited without proper indication (such as ® or ™) after each. Clarification and proper indication of trademarks is required for the following: **TEFLON™**.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The step of vaccinating the patient with a vaccine against the transformed, infected or diseased tissue critical or essential to the practice of the invention is not enabled by the disclosure. The specification does not provide support for the method for inducing an immune response including a step of vaccination along with the removal of components present in the blood. A specific

vaccine against transformed, infected or diseased tissue was not disclosed in the specification as originally filed.

5. Claims 9, 10, and 16-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no descriptive support in the specification as originally filed that the device and method of claims 12 and 1 (from which the rejected claims depend from) is an absorbent column and further, with respect to claims 17 and 18, that the column removed the cytokines or antibody or antibody fragments immunoreactive with the cytokine receptor molecules and that the filter, With respect to claims 10 and 19, that the column had the cytokines or antibody or antibody fragments immobilized thereon. As a result, the disclosure in applicant's original application does not reasonably convey to the artisan that applicant had possession of the time the application was filed of the subject matter in the claims. Thus, the disclosure as originally filed does not satisfy the description requirement in the first paragraph of § 112. See in re Kaslow, 707 F.2d, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983).

6. Claims 21 and 22 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to

make and/or use the invention. The specification as filed fails to provide an enabling disclosure for a kit for treatment of a patient to induce an immune response including a device and an agent. The dispositive issue with regard to the enablement requirement is whether an applicant's disclosure, considering the level of ordinary skill in the art as of the date of applicant's application, would have enabled a person of such skill to make and use the claimed invention without undue experimentation. In re Strahilevitz, 668 F.2d 1229, 1232, 212 USPQ 561, 563 (CCPA 1982). This test is not met for enabling one of ordinary skill in the art to incorporate means for administering radiation (claim 21) or radiation as the agent in a kit for later use (claim 22) in the treatment of a patient for inducing an immune response against transformed, infected or diseased tissue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Since it is established that the claims must define the metes and bounds of the invention with a reasonable degree of precision (In re Venezia), the terms "means for administering radiation" to the tissue (claim 21) and "radiation" is unclear. The definition of "radiation" in Webster's Dictionary is defined as "radiant energy in the form of rays." Thus, it is not clear how "rays" can be physically retained or incorporated into a kit or system for later use in the treatment of a patient.

8. Claims 10 and 19 recite the limitation "the patient's...plasma" passing through the column in lines 3 of the claims. There is insufficient antecedent basis for this limitation in the claim. A patient's plasma was never recited in the method of claims 1 and 12, the claims from which 10 and 19 respectively depend from and further limit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4, 12, 14 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lentz ("Continuous Whole Blood UltraPheresis Procedure in Patients with Metastatic Cancer," 10/15/88). Lentz discloses treating cancer patients having solid tumors by removing components from the blood having molecular weights of less than 150,000 Daltons. Blood was withdrawn from the patients via tubing and passed through a plate filter to remove the components and the filtrate was returned to the patient via tubing. The membrane used had a pore size of 0.05 microns. The treatment was carried out three times per week. Lentz found that the treatment was sufficient to establish and maintain a "tumor inflammatory response." The study showed many patients having tumor necrosis, which inherently reduces the amount of the tumor. Lentz concluded that ultrafiltration alone or in combination with other modalities suggests benefit in the treatment of certain forms of cancer. With respect to claim 20,

the recitation of "wherein the blood is plasma" has not been given patentable weight because it is narrative in form. In order to be given patentable weight, a functional recitation must be expressed as "means" for performing the specified function, as set forth in 35 USC § 112, 6th paragraph, and must be supported by recitation in the claim of sufficient structure to warrant the presence of the functional language (In re Fuller). Therefore, the tubing in the system of Lentz is clearly capable of circulating plasma through the tubing.

10. Claims 1-4, 12, 14 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lentz (4,708,713). Lentz discloses a method and system for inducing an immune response against diseases and conditions which result from or are dependent upon deficiencies in the immune response system. Such diseases or conditions can be cancer or neoplastic tissue (i.e. a tumor). The system includes a filter, inlet and outlet means for connection to a pump, tubing for fluid delivery and return, and a syringe pump which feeds an anti-coagulant to the system to prevent clotting of blood (col. 3, lines 56-68). Lentz's method comprises withdrawing blood from a patient, extracorporeally treating the blood to selectively separate components having a low molecular weight, and returning the treated blood to the patient, which will inherently initiate an immune response against the disease or condition the patient is suffering from. The blood is treated by passing through a filter which removes components having a molecular weight of 200,000 Daltons or less from the blood (col.. 2, lines 8-33). The filter of Lentz will inherently remove components having a molecular weight of

120,000 Daltons or less. Lentz also discloses that the treatment is carried out on multiple occasions. With respect to claim 20, the recitation of "wherein the blood is plasma" has not been given patentable weight because it is narrative in form. In order to be given patentable weight, a functional recitation must be expressed as "means" for performing the specified function, as set forth in 35 USC § 112, 6th paragraph, and must be supported by recitation in the claim of sufficient structure to warrant the presence of the functional language (In re Fuller). Therefore, the tubing in the system of Lentz is clearly capable of circulating plasma through the tubing.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 5, 11, 13-15, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz ('713). Lentz discloses a method and system for inducing an immune response against diseases (see rejection supra).

With respect to claims 13-15, the filter of Lentz is an ultrafiltration filter that is wherein the filter's pore size may be chosen from a range, preferably between 0.03 to about 0.1 microns. It is also taught that the pores may have sizes or geometries similar to those desired components to be removed from the blood, such as circular or non-circular cross sections (col. 4, line 56-col. 5, line 11). With respect to the device being a

capillary membrane with a pore size of about 0.02 and 0.05 microns (claim 13), the device being a parallel plate filter with a pore size of about 0.04 and 0.0 microns (claim 14), and the device having filters with different pores sizes or geometries (claim 15) it would have been obvious to one having ordinary skill in the art to choose a pore size suitable for removing components having a molecular weight of less than 120,000 Daltons since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum range involves only routine skill in the art In re Aller, 105 USPQ 223. With respect to the device being either a capillary membrane or a parallel plate filter, it would have been obvious to one having ordinary skill in the art to substitute either for the ultrafiltration membrane of Lentz to remove components since they are equivalents in the art and perform the same function, the selection of any would have been within the level of ordinary skill in the art.

With respect to claims 5, 11 and 21, the method and system of Lentz including treating the tissue multiple therapies in methods of treating cancer was well known in the art at the time of the invention. It was well known to combine radiation and/or chemotherapy treatments with other methods of cancer treatments at the time of the invention. Therefore, the choice to use a combination of Lentz treatment and system with additional therapy such as vaccine, radiation or chemotherapy would have been obvious at the time of the invention to one of ordinary skill, since it has been held to be within the general skill of a worker in the art, such as the physician in charge of the patient's care, to select a known treatment on the basis of its suitability for the treatment being performed. In re Leshin, 125 USPQ 416.

12. Claims 7-10 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz ('713) in view of Okarma et al. (5,523,096). Lentz discloses the invention substantially as claimed, see rejection supra. Lentz, however, fails to disclose specifically the device being an absorbent column for removing cytokines or TNF from the blood wherein the column has immobilized cytokine fragments through which blood is passed. Okarma et al. discloses an extracorporeal system for removing cytokines from the blood, such as TNF, using an absorption matrix in a column (see col. 3, 3ine 28-col. 4, line 14 & fig. 1B). At the time of the invention, it would have been obvious to combine Lenz and Okarma by substituting the absorbent column of Okarma for the device of Lentz since the removal of cytokines using said column performs an equivalent function, that of removing components from blood. Further, Okarma teaches that the removal of cytokines is done to control the immune system's response to diseases and provide lower circulating levels of cytokines in the blood of a patient.

13. Claims 7, 8, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz ('713) in view of Chen et al. (Journal of Neuropathology and Experimental Neurology). Lentz discloses the invention substantially as claimed, see rejection supra. Lentz, however, fails to disclose specifically the method as removing soluble TNF 1 and 2 receptors from the blood. Chen et al. discloses that soluble TNF receptors help to evade the immune response against a tumor (pg. 549). Therefore, it would have been obvious to a person skilled in the art at the time the invention was

made to carry out the method to remove soluble TNF 1 and 2 by filtration since these molecules evade the immune response against tumors.

14. Claims 5, 6 and 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz ('713) in view of Wolpe (5,861,483). Lentz discloses the invention substantially as claimed, see rejections supra. Lentz also teaches of including a source of anticoagulant in the device. Lentz, however, fails to disclose specifically the device being in a kit and including an agent selected from the group consisting of anti-angiogenic compounds, procoagulant compounds, cytokines, chemotherapeutic agents, and radiation in dosage formulation.

Wolpe, however, discloses the need for stimulatory cytokines, especially erythropoietin, to maintain a fully functional immune system. The methodology that Lentz's method is based on is removing immune inhibitors and letting the body's immune system combat the disease. Therefore, it would have been obvious to a person skilled in the art to add erythropoietin to a kit including Lentz's system since erythropoietin works towards maintaining a fully functional immune system (col. 1, lines 25-45). The system of Lentz on its own is comprised of multiple individual pieces (including a filter, inlet and outlet means for connection to a pump, tubing, a pump, etc.) and is seen as a kit for performing extracorporeal treatment. As the claims are written to a "kit," such kit limitations are met. With respect to claims 23, 24, 27 and 28, the combination of Lentz and Wolpe disclose the invention except for the use of chemotherapeutic agents, progoagulant compounds, or anti-angiogenic compounds.

To one of ordinary skill in the art, it would have been obvious to replace the erythropoietin with one of the above listed agents since it has been held to be within the general skill of a worker in the art, such as the physician in charge of the patient's care, to select a known agent or compound on the basis of its suitability for the treatment being performed. In re Leshin, 125 USPQ 416.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

15. A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-6, 12-16 and 20-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6, and 8-22 of copending Application No. 09/083,307. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims are identical. To overcome this rejection one set of claims must be cancelled.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7, 8-10, and 12-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 10-19 of U.S. Patent No. 6,231,536. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the application recite a broader view of patented claims. Patent method claim 1 is identical to application claims (1, 7 & 8) and patent system claim 10 is identical to application claims (12, 16 & 17). Therefore, the patent anticipates the claims and if a patent were to issue on the pending claims applicant would be granted an improper timewise extension of the patent term.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Howell et al. ('708) discloses an analogous method and system for enhancing immune response in mammals and Nakatani et al. ('898) discloses an analogous column for removing TNF from blood.

Any inquiry concerning the rejections contained within this communication or earlier communications should be directed to examiner Tricia Bianco whose telephone number is (703) 305-1482. The examiner can normally be reached on Monday through Fridays from 9:00 AM until 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Angela Sykes can be reached on (703) 308-5181. The official fax numbers for the organization where this application or proceeding is assigned is (703) 872-9302 for regular communications and for After Final communications (703) 872-9303.

Tricia Bianco
Patent Examiner
Art Unit 3762

pmb
October 17th, 2002